EBTM
Encontro de
Biotecnologia Medicinal

ICMB
Iberian Congress on
Medicinal Biotechnology

BOOK OF ABSTRACTS

P.PORTO ESCOLA SUPERIOR DE SAÚDE

2 ICMB
Iberian Congress on
Medicinal Biotechnology

5 EBTM
Encontro de
Biotecnologia Medicinal

21 OCT 2022

P.PORTO ESCOLA SUPERIOR DE SAÚDE

Peptide-ionic liquid conjugates towards the treatment of skin infections

Ana Gomes [1], Lucinda Bessa[1,2], Iva Fernandes[1], Cátia Teixeira[1,3], Luisa Aguiar[1,3], Ricardo Ferraz[1,4], Cláudia Monteiro[4,5], Cristina Martins[5,6,7], Nuno Mateus[1], Paula Gameiro[1], Paula Gomes[1]

1. REQUIMTE, Departamento de Química e Bioquímica, Faculdade de Ciências, Universidade do Porto, Portugal. **2.** current affiliation: CIIEM, Egas Moniz - Cooperativa de Ensino Superior, Almada, Portugal, **3.** current affiliation: Gyros Protein Technologies, Tucson, AZ 85714, United States of America. **4.** CQBM, Escola Superior de Saúde, Politécnico do Porto, Portugal. **5.** i3S - Instituto de Investigação e Inovação em Saúde, Universidade do Porto, Portugal. **6.** INEB - Instituto de Engenharia Biomédica, Porto, Portugal. **7.** ICBAS - Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto, Portugal.

The treatment of complicated skin infections, like diabetic foot ulcers and other chronic wounds, are often associated with persistent polymicrobial biofilms that delay and difficult the healing process.[1] The most severe cases culminate in inpatient hospital admission, where infections can be exacerbated by hospital-acquired pathogens, in particular, if caused by the so-called ESKAPE pathogens, for which few efficient antibiotics are available.[2] The current biomedical approaches to chronic wounds aim at providing both protection against multidrug-resistant (MDR) bacteria and a matrix scaffold, often collagen-based, to boost the reestablishment of healthy skin.[3] Therefore, new options and new antibiotics are urgently needed and having that in mind our strategy is to use: i) antimicrobial peptides (AMP) to prevent or treat infection in the open wound; ii) collagen-inducing peptides (CBP)[4] to induce fast healing; iii) and ionic liquids (IL) [5] with intrinsic antimicrobial chemical permeation enhancement properties for an improved skin permeation. Through different combinations of these three types of building blocks, we aim to find a new class of active pharmaceutical ingredients suitable for topical application in the treatment of complicated skin infections. All the different conjugates designed and tested in vitro thus far will be presented.[6-8] The most promising ones result from conjugation of CBP with IL, delivering a new type of conjugate with potent antibacterial, antifungal, and collagen-inducing effects on human dermal fibroblasts.[9] Hence, these peptide-ionic liquid conjugates are promising leads towards the development of a topical formulation for the treatment of complicated skin infections.

Keywords: skin infections, antimicrobial peptide, ionic liquid, wound healing

References:

1. Leong, H.N.; Kurup, A.; Tan, M.Y.; Kwa, A.L.H.; Liau, K.H.; Wilcox, M.H. Management of complicated skin and soft tissue infections with a special focus on the role of newer antibiotics. Infect Drug Resist 2018, 11, 1959-1974, doi:10.2147/IDR.S172366.

2. Mulani, M.S.; Kamble, E.E.; Kumkar, S.N.; Tawre, M.S.; Pardesi, K.R. Emerging Strategies to Combat ESKAPE Pathogens in the Era of Antimicrobial Resistance: A Review. Front Microbiol 2019, 10, 539-539, doi:10.3389/fmicb.2019.00539.

3. Holmes, C.; Wrobel, J.S.; Maceachern, M.P.; Boles, B.R. Collagen-based wound dressings for the treatment of diabetes-related foot ulcers: a systematic review. Diabetes, metabolic syndrome and obesity : targets and therapy 2013, 6, 17-29, doi:10.2147/dmso.s36024.

4. Gomes, A.; Teixeira, C.; Ferraz, R.; Prudencio, C.; Gomes, P. Wound-Healing Peptides for Treatment of Chronic Diabetic Foot Ulcer and Other Infected Skin Injuries. Molecules 2017, 22, doi:10.3390/molecules22101743.

5. Gomes, A.; Aguiar, L.; Ferraz, R.; Teixeira, C.; Gomes, P. The Emerging Role of Ionic Liquid-Based Approaches for Enhanced Skin Permeation of Bioactive Molecules: A Snapshot of the Past Couple of Years. International Journal of Molecular Sciences 2021, 22, doi:10.3390/ijms222111991.

6. Gomes, A.; Bessa, L.J.; Correia, P.; Fernandes, I.; Ferraz, R.; Gameiro, P.; Teixeira, C.; Gomes, P. "Clicking" an Ionic Liquid to a Potent Antimicrobial Peptide: On the Route towards Improved Stability. Int. J. Mol. Sci. 2020, 21, 1-11, doi: https://doi.org/10.3390/ijms21176174.

7. Gomes, A.; Bessa, L.J.; Fernandes, I.; Ferraz, R.; Mateus, N.; Gameiro, P.; Teixeira, C.; Gomes, P. Turning a Collagenesis-Inducing Peptide Into a Potent Antibacterial and Antibiofilm Agent Against Multidrug-Resistant Gram-Negative Bacteria. Front Microbiol 2019, 10, 1-11, doi:10.3389/fmicb.2019.01915.

8. Gomes, A.; Bessa, L.J.; Fernandes, I.; Ferraz, R.; Monteiro, C.; L. Martins, M.C.; Mateus, N.; Gameiro, P.; Teixeira, C.; Gomes, P. Disclosure of a Promising Lead to Tackle Complicated Skin and Skin Structure Infections: Antimicrobial and Antibiofilm Actions of Peptide PP4-3.1. Pharmaceutics 2021, 13, doi:10.3390/pharmaceutics13111962.

9. Gomes, A.; Bessa, L.J.; Fernandes, I.; Aguiar, L.; Ferraz, R.; Monteiro, C.; Martins, M.C.L.; Mateus, N.; Gameiro, P.; Teixeira, C.; et al. Boosting Cosmeceutical Peptides: Coupling Imidazolium-Based Ionic Liquids to Pentapeptide-4 Originates New Leads with Antimicrobial and Collagenesis-Inducing Activities. Microbiology spectrum 2022, 10, e0229121, doi:10.1128/spectrum.02291-21.